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## Adrenal Cytomegaly: Two Cases Detected by Prenatal Diagnosis

**Shin-ichi Noguchi, Kouji Masumoto, Tomoaki Taguchi, Yukiko Takahashi,<sup>1</sup> Masazumi Tsuneyoshi<sup>1</sup> and Sachiyo Suita**, Departments of Pediatric Surgery and <sup>1</sup>Anatomic Pathology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan.

We report our experience with two cases of adrenal cytomegaly, both of which were detected as cystic adrenal masses during prenatal ultrasonographic examinations. In Case 1, a left suprarenal cystic mass was detected in the fetus at 25 weeks of gestation. The mass, measuring 7 cm in diameter, did not show any change in size and was resected 26 days after birth. In Case 2, a right suprarenal lesion was found at 30 weeks of gestation. The cystic lesion, measuring 2 cm × 1.5 cm, did not change in size and was resected 3 months after birth. Adrenal cytomegaly is still not well known. It is characterized by the presence of large polyhedral cells with eosinophilic granular cytoplasm and enlarged nuclei in the adrenal cortex. This condition is thought to be a degenerative process but not a malignancy. Adrenal cytomegaly rarely forms cysts. It seemed to be impossible to diagnose preoperatively in our cases. Because of the difficulty of differentiating between cystic adrenal cytomegaly and other cystic diseases such as neuroblastoma, operative intervention is required in cases where the cysts do not decrease in size. Further study of a larger number of cases is needed to establish an optimal treatment protocol for these tumours. [*Asian J Surg* 2003;26(4):234–6]

### Introduction

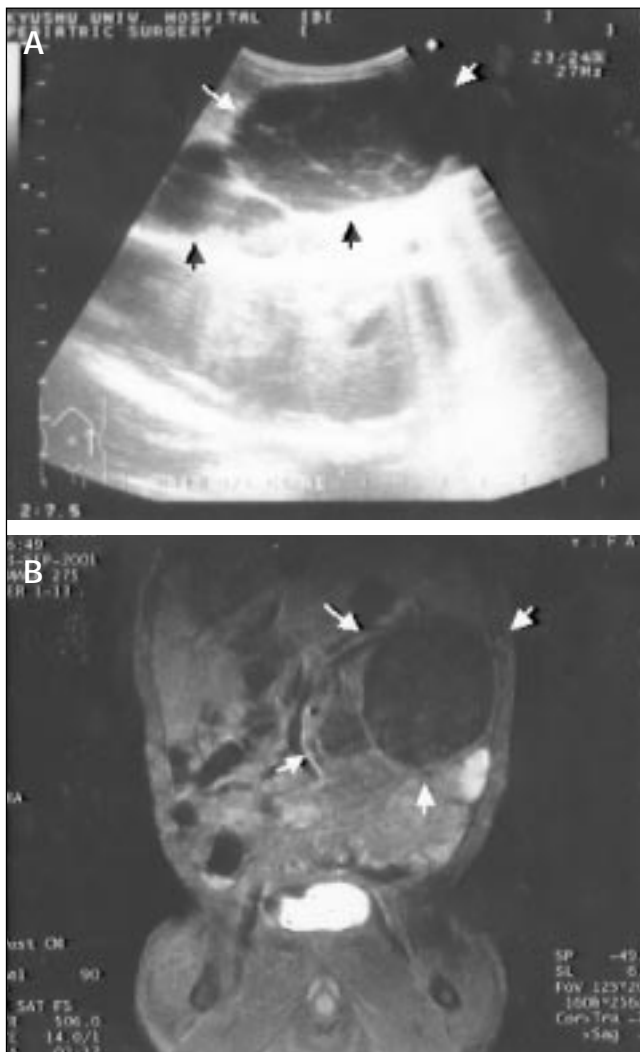
Owing to the continuing advances in prenatal ultrasound examinations, many masses are now being found in fetuses.<sup>1</sup> In some cases, however, management is difficult due to difficulties in making a definite diagnosis. In particular, cystic suprarenal lesions are more difficult to manage since such lesions may be due to adrenal haemorrhage, neuroblastoma, or other diagnoses.<sup>1</sup> We report our experience with two cases of suprarenal cystic lesions found prenatally. The diagnosis was adrenal cytomegaly in both cases. Adrenal cytomegaly refers to the presence of large polyhedral cells with eosinophilic granular cytoplasm and enlarged nuclei in the adrenal cortex of newborn infants.<sup>2,3</sup> This entity is still not well known. Our two cases of cystic adrenal cytomegaly are described.

### Case reports

#### Case 1

A left suprarenal cystic mass was detected in the fetus on routine sonogram performed at 25 weeks' gestation. Though the mass gradually increased in size, the baby was born safely by normal vaginal delivery. There was no family history of childhood malignancy except for his uncle who had a malignant schwannoma. Ultrasound examination and magnetic resonance imaging (MRI) of the newborn confirmed the cystic mass, which measured 7 cm at its greatest dimension (Figure 1). No other abnormalities, such as hemihypertrophy, were noted. Urine vanillylmandelic acid (VMA) and homovanillic acid (HVA) concentrations were within normal ranges. Repeat sonography every day did not show any change in the size of the mass. The infant underwent total excision of the mass at

Address correspondence and reprint requests to Dr. Shin-ichi Noguchi, Department of Pediatric Surgery, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan.  
E-mail: [noguh@pedsurg.med.kyushu-u.ac.jp](mailto:noguh@pedsurg.med.kyushu-u.ac.jp) • Date of acceptance: 1<sup>st</sup> May, 2003



**Figure 1.** Case 1. A) Ultrasonography of the abdomen reveals several cystic lesions with septa. B) Magnetic resonance imaging shows two cystic lesions in the left side of the upper abdomen.

26 days of age. Histopathologically, the cyst wall was composed of fetal adrenal cortex with enlarged cells demonstrating large irregular hyperchromatic nuclei and abundant eosinophilic cytoplasm (Figure 2). No signs of recurrence were observed for 12 months.

### Case 2

Routine sonogram revealed a right adrenal mass in the fetus at 30 weeks' gestation. The mass could not be seen at 37 gestational weeks. However, ultrasound examination and MRI in the newborn male infant showed a cystic mass that measured 2 cm at its greatest dimension (Figure 3A). The baby had no family history of childhood malignancy and showed no signs of Beckwith-Wiedemann syndrome. Urine VMA and HVA concentrations were within normal ranges. Three months later, the cystic mass was resected at his parents' request. The his-

topathological diagnosis was adrenal cytomegaly (Figure 3B). At follow-up at 7 months, no signs of recurrence were observed on abdominal sonography and computed tomography.

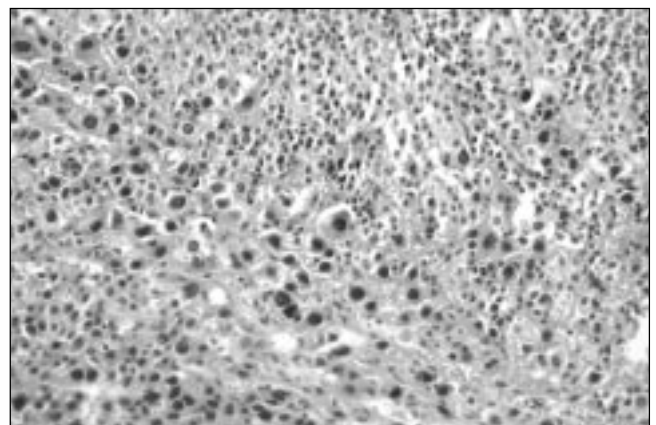
### Discussion

In the adrenal cortex of newborn infants, occasionally distinct, large cells, with large, prominent nuclei can be found. This phenomenon is called adrenal cytomegaly. This condition was first described in the fetal adrenal cortex by Kampmeier in 1927.<sup>2</sup> Its incidence ranges from 6.5% of necropsies in newborns to 0.1%, but there are probably many cases with minimal changes.<sup>3</sup> It has only rarely been found in adults.<sup>4</sup>

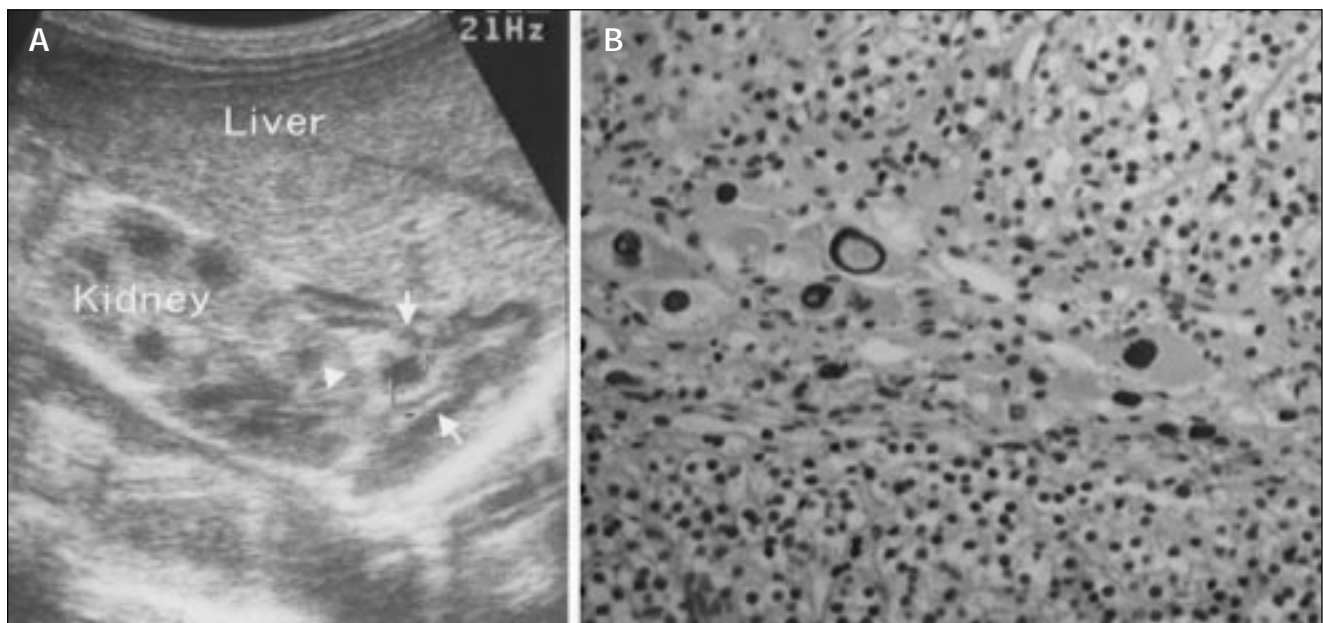
Cytomegalic cells have large, irregularly shaped, hyperchromatic nuclei, and eosinophilic cytoplasm that contain numerous vacuoles. They are distributed diffusely or focally in the fetal zone of the adrenal cortex. In an electron microscopy study of cytomegalic cells, the nuclear inclusions were invaginations of the cytoplasm, and viral particles could not be found.<sup>5</sup> Moreover, cytomegalic cells have very low proliferative activity, so this entity is thought to be a degenerative process but not a malignancy.<sup>6</sup>

Adrenal cytomegaly is also known to be associated with various syndromes, including congenital adrenal hypoplasia, erythroblastosis fetalis, and Beckwith-Wiedemann syndrome.<sup>3</sup> The criteria for Beckwith-Wiedemann syndrome include adrenal cytomegaly and omphalocele, macroglossia, hyperplasia of gonadal interstitial cells, renal medullary dysplasia, and hyperplastic visceromegaly.

In cases of adrenal cytomegaly, cystic lesions are rarely formed. As far as we could determine, only one previous case



**Figure 2.** Case 1. Microscopically, the cyst wall is composed of fetal adrenal cortex admixed with enlarged cells demonstrating large irregular hyperchromatic nuclei and an abundance of eosinophilic cytoplasm.



**Figure 3.** Case 2. A) Ultrasonography of the abdomen reveals a small cystic lesion above the right kidney. B) Microscopically, some enlarged cells have pseudoinclusions in their nuclei.

has been reported to demonstrate cystic lesions.<sup>7</sup> This case was associated with incomplete Beckwith-Wiedemann syndrome. Neither of our cases was associated with Beckwith-Wiedemann syndrome. As a result, these two cases are considered the first reported cases of cystic adrenal cytomegaly that are not associated with Beckwith-Wiedemann syndrome (Table).

The increasing use of abdominal ultrasonography during pregnancy is leading to the discovery of an increasing number of suprarenal masses. Neuroblastoma is the most frequent neonatal malignancy, but suprarenal masses can also be ascribed to adrenal haemorrhage.<sup>1</sup> The optimal diagnosis and treatment of these masses has not yet been determined. In our cases, cystic neuroblastomas were preoperatively suspected. Urinary VMA and HVA concentrations may increase in cases of neuroblastoma. However, regarding neuroblastomas diagnosed during the perinatal period, the sensitivity of these tumour markers is 52% (14/27).<sup>1</sup> The differential diagnosis for cystic adrenal cytomegaly and cystic neuroblastoma remains quite difficult. We believe that surgical intervention is required in cases where there is no decrease in size after 1 or 2

months' observation. A larger number of cases needs to be investigated in order to establish an optimal treatment protocol for these tumours.

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**Table.** Summary of reported cases with cystic adrenal cytomegaly

Case	Prenatal diagnosis	Site	Age at operation	Cyst size (cm)	B-W syndrome
2-day-old boy <sup>7</sup>	No	Bilateral	35 d	R: 3 × 4 × 4; L: 4 × 5 × 6	Incomplete type
Case 1	25 wk	Left	26 d	7 × 5.5 × 3.5	-
Case 2	30 wk	Right	3 mo	2 × 1.5	-

B-W = Beckwith-Wiedemann; R = right; L = left.